510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k121397

B. Purpose for Submission:

Clearance of new device

C. Measurand:

Human hemoglobin (hHb) in human feces

D. Type of Test:

Qualitative

E. Applicant:

Sekisui Diagnostics, LLC

F. Proprietary and Established Names:

OSOM® iFOB Test

OSOM® iFOBT Control Kit

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.6550; Occult blood test

2. Classification:

   Class II

3. Product code:

   KHE, Reagent, Occult blood

4. Panel:

Hematology (81)

H. Intended Use:

1. Intended use(s):

   The OSOM iFOB (Immunochemical Fecal Occult Blood) Test is a rapid immunoassay for the qualitative detection of fecal occult blood by laboratories or physicians' offices. It is useful for the detection of human hemoglobin in human fecal samples and is recommended for use as part of routine physical examinations or when lower gastrointestinal disorders are suspected.

   The OSOM iFOBT Control Kit is intended for use in quality control testing with the OSOM iFOB Test.

2. Indication(s) for use:

   Same as intended use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Control Kit is intended for use only with the OSOM iFOB Test.

I. Device Description:

The OSOM iFOB (Immunochemical Fecal Occult Blood) Test is a rapid test which can detect the presence of occult blood in human fecal samples by detecting the presence of human hemoglobin (hHb). The OSOM iFOB Test is a qualitative assay that employs immuochromatographic, lateral flow technology. A test kit contains 25 pouched Test Devices, 25 Extraction Reagent vials, 25 conjugate vial tips, and 25 sample collection packs. Tests and Reagents are also available in a 50-test kit without sample collection packs, and sample collection packs are available separately in a package of 50. Negative and positive external controls are provided separately as the OSOM iFOBT Control Kit.

Control Description: The OSOM iFOBT Control Kit includes a Negative Control and a Positive Control. The Negative Control is free of detectable human hemoglobin and the Positive Control contains human hemoglobin sufficient to provide a positive result when used with the OSOM iFOB Test. The Controls are used for external quality control as an aid in verifying test and operator performance.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Alfa Scientific Designs' Instant-View Fecal Occult Blood Rapid Test (currently marketed as Quidel QuickVue iFOB Test).

2. Predicate 510(k) number(s):

   k021423

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	A rapid immunoassay for the qualitative detection of fecal occult blood by laboratories or physicians' offices. It is useful for the detection of human hemoglobin in human fecal samples and is recommended for use as part of routine physical examinations or when lower gastrointestinal disorders are suspected.	An immunochemical device intended for the qualitative detection of Fecal Occult Blood by laboratories or physicians' offices. It is useful in determining gastrointestinal (GI) bleeding found in a number of GI disorders, such as diverticulitis, colitis, polyps, and colorectal cancer. Recommended for use in routine physical examinations, hospital monitoring for bleeding patients, and screening for colorectal cancer or GI bleeding from any source.
Specifically detecting	Qualitative human hemoglobin (hHb)	Qualitative human hemoglobin (hHb)
Specimen	Human fecal specimen	Human fecal specimen
Detection Level	Immunochromatographic membrane assay	Immunochromatographic membrane assay
Capture Antibody	Polyclonal Goat anti-hHb	Anti-hHb antibodies
External Controls	Negative: Buffer solution Positive: hHb in buffer solution provided separately	Negative: Buffer solution Positive: hHb in buffer solution provided separately

Differences		
Item	Device	Predicate
Detection Antibody Conjugate	Monoclonal mouse anti-hHb conjugated to blue latex	Monoclonal mouse anti-hHb conjugated to colloidal gold
Result Format	Negative: Visible red control line	Negative: Single visible burgundy line
	Positive: Visible red control line and visible blue test line	Positive: 2 visible burgundy lines
Internal Control	Visible red control line	Visible burgundy line
Sample Collection and Transport	Provided applicator stick is used to collect a small portion of feces and apply to sample collection card. Dry card is transported in mailing envelope	Provided grooved sample collection probe is used to collect fecal sample which is inserted in buffer tube. Buffer tube is transported in mailing envelope
Sensitivity to Hemoglobin Variants	Hb S: 50 ng/mL Hb C: 50 ng/mL	Data not available
Time to Result	5 minutes	5-10 minutes

K. Standard/Guidance Document Referenced (if applicable):

FDA's Guidance for Industry and FDA staff: Review Criteria for Assessment of Qualitative Fecal Occult Blood In Vitro Diagnostic Devices; August 8, 2007.

L. Test Principle:

The OSOM iFOB (Immunochemical Fecal Occult Blood) Test is a rapid test which can detect the presence of occult blood in human fecal samples by detecting the presence of human hemoglobin (hHb). The OSOM iFOB Test is a qualitative assay that employs immunochromatographic, lateral flow technology. The fecal sample collected using an OSOM iFOB sample collection card is placed into a prefilled vial containing extraction buffer. This test solution is then dispensed, through a dropper tip containing human hemoglobin antibody conjugated to latex, into the sample well of the test device. The sample migrates across the membrane containing a Test line coated with anti-human hemoglobin antibody and a Control line. If hemoglobin is present at or above the level of detection of the test, an antigen/antibody complex will be formed. The appearance of a visible blue Test line and a red Control line in the result window indicates the presence of human hemoglobin in the sample. A red control line must appear for the results to be valid. If a detectable level of hemoglobin is not present, only the red Control line will appear in the result window. An invalid test occurs when no control line appears.

The Control line serves as an internal procedural control, indicating that the test system is functioning correctly and that the operator added a sufficient volume of sample. In addition to the internal control in each test device, external controls are available in a separate OSOM iFOBT control kit. The Negative Control (buffer solution) and the Positive Control (hHb in buffer solution) are run in the iFOB Test in the same manner as an extracted fecal sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

To demonstrate the reproducibility of the OSOM iFOB Test, an evaluation was conducted at three external physician office laboratories (POL) and one internal site using three OSOM test kit lots. Each site tested randomly coded panels of fecal samples spiked with human blood, with known concentrations of hemoglobin A (HbA) at five different concentrations: 0, 37.5, 50, 62.5, and 2000 ng/mL.

Testing was performed at the external POL sites by 3 intended users per site, with varying levels of education and work experience. Testing at Sekisui Diagnostics was performed by two experienced laboratory professionals. Each panel consisted of 15 test samples, 3 of each of the 5 hemoglobin concentration levels, dried onto an OSOM iFOB sample collection card. Each POL operator tested, in a random fashion, 1 panel on each of the 3 lots of the OSOM iFOB Test. The internal site tested the same number of samples across the 3 lots, with the panels divided between the two operators. Testing was performed over three non-consecutive days and all operators were blinded to the test sample analyte levels.

The results obtained by the three POL sites and the reference laboratory had an overall agreement of 98.5% (95% CI: 97.4 – 99.0%) to the expected results, with a positive percent agreement of 98.5% (95% CI: 96.4 – 99.3%), and a negative percent agreement of 98.6% (95% CI: 96.0 – 99.5%). A summary of the reproducibility study result is provided in the table below.

OSOM iFOB Reproducibility test results

	Expected		
OSOM	**Positive**	**Negative**	**Total**
Positive	320	3	323
Negative	5	214	219
Total	325	217	542

b. Linearity/assay reportable range:

Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The device and controls are not traceable to any recognized reference materials.

Internal Control: Procedural controls are included in the test device. The control line serves as an internal procedural control, indicating that the test system is functioning correctly and that the operator added a sufficient volume of sample.

External Quality Control: In addition to the internal control in each test device, external controls are available in a separate OSOM iFOBT control kit. The negative control (buffer solution) and the positive control (hHb in buffer solution) are run in the iFOB Test in the same manner as an extracted fecal sample. It is recommended that positive and negative controls be performed to verify proper test performance.

Sample Stability: Fecal samples with negative (0 ng/mL hHbA) and positive (50 ng/mL hHbA) were applied to sample collection cards, dried, and stored in mailing envelopes at room temperature for 46 days. Testing was performed (n=5) at intervals with the OSOM iFOB Test. All positive samples were positive and all negative samples were negative, demonstrating that fecal sample is stable for 46 days when stored at room temperature.

Sample Shipping Stress test: To assess the effects of exposure to transportation stress and environmental extremes on the stability of dried fecal samples, negative (0 ng/mL hHbA) and positive (50 ng/mL hHbA) fecal samples were prepared, applied to sample collection cards, dried, and placed in mailing envelopes. In evaluating the effect of exposure to elevated temperatures, fecal samples were stored for 8 hours at 50°C, 55°C, and 60°C and for 2 days at 45°C. To evaluate the effect of low temperature exposure, samples were stored for 2 days at 2 - 8°C and 2 days at -20°C with two freeze/thaw cycles. Stressed samples were tested (n=5) with the OSOM iFOB Test. All results were acceptable, demonstrating that dried fecal samples are stable in the mailing envelope up to 8 hours at temperatures as high as 60°C and up to 2 days at temperatures as low as -20° C with up to two freeze/thaw cycles.

iFOB Test Kit Stability Study: Real time stability of the device (cassette, conjugate vial tips, extraction reagent vials) was tested with 3 lots of the device. Devices were stored at ambient room temperature (25°C) for ten months. Three devices from each lot were tested with spiked fecal samples at time points 0, 9, and10 months in support of an initial nine months shelf-life. All test results were acceptable demonstrating an initial stability of nine months when store at room temperature. Stability testing with spiked fecal samples, in triplicate will continue for the duration of the stability study to extend the expiration dating based on passing stability results.

iFOB Test Kit Shipping Stress Test: To evaluate the effect of exposure to elevated temperatures, iFOB reagents were stored for 8 hours at 50°C, 55°C, and 60°C and for 2 days at 45°C. To evaluate the effect of low temperature exposure, reagents were stored for 2 days at 2 - 8°C and 2 days at -20°C with two freeze/thaw cycles. Reagents were also stored at room temperature (unstressed) as a control condition. Spiked fecal samples and liquid hemoglobin controls (negative and low level positive HbA control) were then tested with these stored reagents. At zero time point testing was performed with five replicates and testing was performed in triplicate for other time points. All test results were acceptable, demonstrating that iFOB Test Kit performance was unaffected by the extreme temperatures tested.

iFOBT Control Kit Stability Study: Shelf life for iFOBT Controls was estimated by accelerated stability testing of two lots of controls conducted at 2-8°C, 25°C and 37°C. Testing was performed with one lot of iFOB Test reagents and included five replicates on day zero and three replicates on all other days. The observed accelerated stability results for 65 days of testing predict 24 months shelf life for the OSOM iFOBT Control Kit at a storage temperature of 2° to 8°C. Accelerated stability studies will continue up to 100 days, and confirmatory real time stability studies at 2° to 8°C and at room temperature will continue for 24 months.

In addition to studies to determine expiry dating, open vial stability studies were performed for the iFOB Controls. Three vials each of two lots of the negative and positive controls were tested after opening on day zero, vials were re-capped and stored at room temperature. Testing of all vials was performed in triplicate on day-15 and day-31. All results were acceptable, demonstrating 30 days open vial stability at room temperature.

iFOBT Control kit Shipping Stress Test: iFOBT test kits and two lots of the control (positive and negative) stored at 50°C, 55°C, 60°C for 4 and 8 hours and at 45°C for 2 days were tested. Effect of low temperature exposure was evaluated by storing controls at 2 - 8°C for 2 days and at -20°C for 2 days with two freeze/thaw cycles. Control materials were also stored at room temperature (unstressed) as a control condition. At zero time point testing was performed with five replicates and testing was performed in triplicate at other time points. Test results showed that positive and negative controls were not stable at 60°C and stable at all other conditions tested.

d. Detection limit:

The detection limit of the device was determined by spiking hemoglobin free stool samples with known concentrations of hemoglobin A at five different concentrations: 0, 37.5, 50, 62.5 and 2000 ng hHb/mL. The cut-off level was determined to be 50 ng hHb/mL and no prozone effect was seen at up to 2000 ng hHb/mL.

e. Analytical specificity:

The ability of the OSOM iFOB Test to detect human hemoglobin variants was demonstrated in testing of known levels of hemoglobin-S (HbS) and hemoglobin-C (HbC) across three reagent lots. All three lots of iFOB Test detected the presence of both HbS and HbC at concentrations of 50 ng/mL and higher.

Cross-Reactivity

The following non-human hemoglobin and meat extracts were added to specimens negative for human hemoglobin. The substances at the concentrations listed below did not interfere with the test results.

Substance	**Concentration**
Human Mb	500 µg/mL
Sheep Hb	500 µg/mL
Horse Hb	500 µg/mL
Bovine Hb	2,000 µg/mL
Porcine Hb	500 µg/mL
Chicken Hb	500 µg/mL
Rabbit Hb	500 µg/mL
Fish Hb	500 µg/mL
Goat Hb	500 µg/mL
Horse Mb	500 µg/mL
Sheep meat extract	500 µg/mL
Beef meat extract	500 µg/mL
Pig meat extract	500 µg/mL
Chicken meat extract	500 µg/mL
Rabbit meat extract	500 µg/mL
Fish meat extract	500 µg/mL
Goat meat extract	500 µg/mL

Interfering Substances

The following potentially interfering substances were added to specimens containing 0 or 50 ng/mL of human hemoglobin. The substances at the concentrations listed below did not interfere with the test results.

Substance	**Concentration**
Horseradish Peroxidase	20,000 µg/mL
Broccoli (aqueous extract)	Aqueous extract
Turnip (aqueous extract)	Aqueous extract
Parsnip (aqueous extract)	Aqueous extract
Cauliflower (aqueous extract)	Aqueous extract
Cantaloupe (aqueous extract)	Aqueous extract
Red radish (aqueous extract)	Aqueous extract
Vitamin C, 0.25 mg/mL	Dietary supplement

Iron, 0.065 mg/mL	Dietary supplement

Hook Effect

Samples with elevated levels of hHbA, hHbS and hHbC at the following concentration (200 ng/mL, 500 ng/mL, 1000 ng/mL and 2,000 ng/mL) were prepared and tested with three lots of OSOM iFOB reagents. Results for all samples were positive, demonstrating that there is no hook (prozone) effect at hemoglobin levels of 200 ng/mL, 500 ng/mL, 1000 ng/mL or 2,000 ng/mL.

f. Assay cut-off:

The assay cut-off is 50 ng/mL of human hemoglobin in feces.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed to compare the performance of OSOM iFOB Test to a commercially available predicate device, Alfa Instant-View FOB Rapid Test (K021423), currently marketed as Quidel QuickVue iFOB Test. Fecal samples were spiked with human blood with known concentrations of HbA at five different concentrations (0, 37.5, 50, 62.5, and 2,000 ng/mL). Samples were applied to OSOM iFOB sample collection cards, dried, and tested with the OSOM iFOB Test. Samples for QuickVue testing were transferred to the provided collection tube according to the QuickVue instructions and tested with the QuickVue iFOB Test. Twenty-five replicates of each hemoglobin concentration were tested with OSOM iFOB reagents and QuickVue iFOB Test. Summaries of the QuickVue iFOB and OSOM iFOB results by lot number are shown in the tables below:

Quidel QuickVue iFOB: 20 Devices Test Cassette Lot # 204372 and Collection Tube Lot # 028830				
Hemoglobin Concentration	**Number Negative**	**Number Positive**	**Agreement with Expected (%)**	**95% Confidence Interval**
0 ng/mL	20	0	100.0	83.2 - 100.0
37.5 ng/mL	20	0	100.0	83.2 - 100.0
50.0 ng/mL	0	20	100.0	83.2 - 100.0
62.5 ng/mL	0	20	100.0	83.2 - 100.0
2,000 ng/mL	0	20	100.0	83.2 - 100.0

Quidel QuickVue iFOB: 5 Devices Test Cassette Lot # 202661 and Collection Tube Lot # 028234				
Hemoglobin Concentration	**Number Negative**	**Number Positive**	**Agreement with Expected (%)**	**95% Confidence Interval**
0 ng/mL	5	0	100.0	47.8 - 100.0
37.5 ng/mL	5	0	100.0	47.8 - 100.0
50.0 ng/mL	0	5	100.0	47.8 - 100.0
62.5 ng/mL	0	5	100.0	47.8 - 100.0
2,000 ng/mL	0	5	100.0	47.8 - 100.0

OSOM iFOB: 25 Devices Test Cassette Lot # 111228, Conjugate Tips Lot # 81-26 and Extraction Reagent Lot # 111608				
Hemoglobin Concentration	**Number Negative**	**Number Positive**	**Agreement with Expected (%)**	**95% Confidence Interval**
0 ng/mL	25	0	100.0	86.3 - 100.0
37.5 ng/mL	24	1	96.0	79.6 - 100.0
50.0 ng/mL	0	25	100.0	86.3 - 100.0
62.5 ng/mL	0	25	100.0	86.3 - 100.0
2,000ng/mL	0	25	100.0	86.3 - 100.0

Overall result agreement of OSOM iFOB with QuickVue was determined to be 99.2% (95% CI: 96.0 – 99.5%). Positive agreement was 100% (95% CI: 95.1 – 100.0%) and negative agreement was 98.0% (95% CI: 89.5 0 99.6%). A summary of the total combined comparison result is provided in the table below.

Comparison of OSOM iFOB Test to Predicate device (Quidel QuickVue)

	Quidel QuickVue		
OSOM	**Positive**	**Negative**	**Total**
Positive	75	1	76
Negative	0	49	49
Total	75	50	125

The above method comparison study demonstrated that the analytical performance of OSOM iFOB Test is substantially equivalent to the predicate device.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The OSOM iFOB Test will produce positive results when ≥50 ng/mL of hHb is present in human fecal samples and negative when <50 ng/mmL of hHb is present.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.